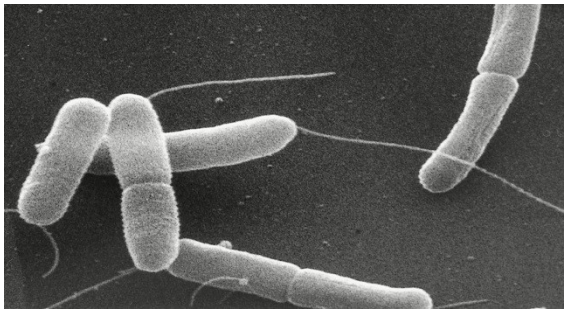
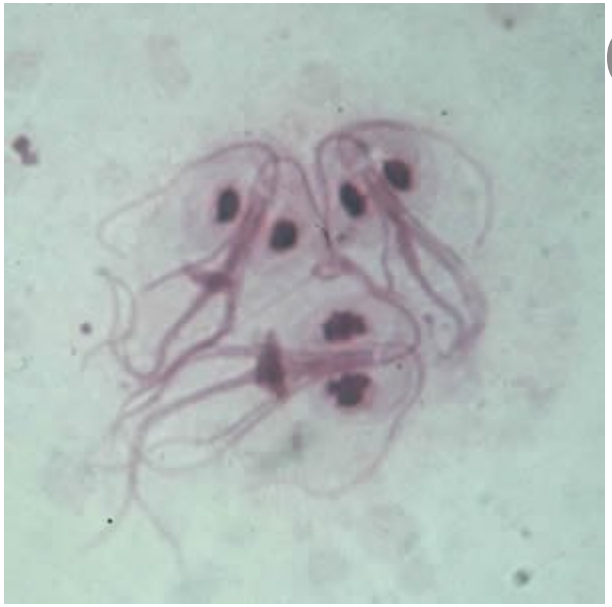
WRAIR
Walter Reed Army Institute of Research
Soldier Health • World Health

Uniformed Services University
of the Health Sciences



Infectious Diarrhea in Travel and Military



OL Kent E. Kester

October 2013

Definition of Travelers' Diarrhea

- Cramps, nausea, vomiting, fever, blood in stools
- Classic – passage of > 3 unformed stools in 24 hours plus at least one of above symptoms
  - Moderate: 1-2 unformed stools in 24 hours plus one of above symptom
  - Mild: passage of one or two unformed stools in 24 hours without other symptoms
- Typically acquired within first few weeks of travel/ deployment.

Impact of Diarrheal Diseases in Modern Military Campaigns

- **World War II**: ‘A few months of the year, malaria would cause more man-days lost, but on the calendar-year average, gastrointestinal infections were well ahead.’[1]
- **Vietnam War**: Diarrhea/dysentery largest single disease threat, leading to 4 times more hospitalizations than malaria[2]
- **OIF**: Acute enteric illness was leading cause of hospital admission among British forces during first 12 months of operations in Iraq[3]

(1) Ward TG: *History of Preventive Medicine*, US Army Forces in the Middle East, 19Oct41 - 23Jun44, Vol. 111. [Official record.]

(2) Wells RF, GI Diseases: Background and Buildup. In: Internal Medicine in Vietnam Vol II: General Medicine and ID, US Army Medical Dept 0:345-354.

(3) Grange, C: J Royal Army Medical Corps, 2005:151(2):101-104.

Force Health Impacts

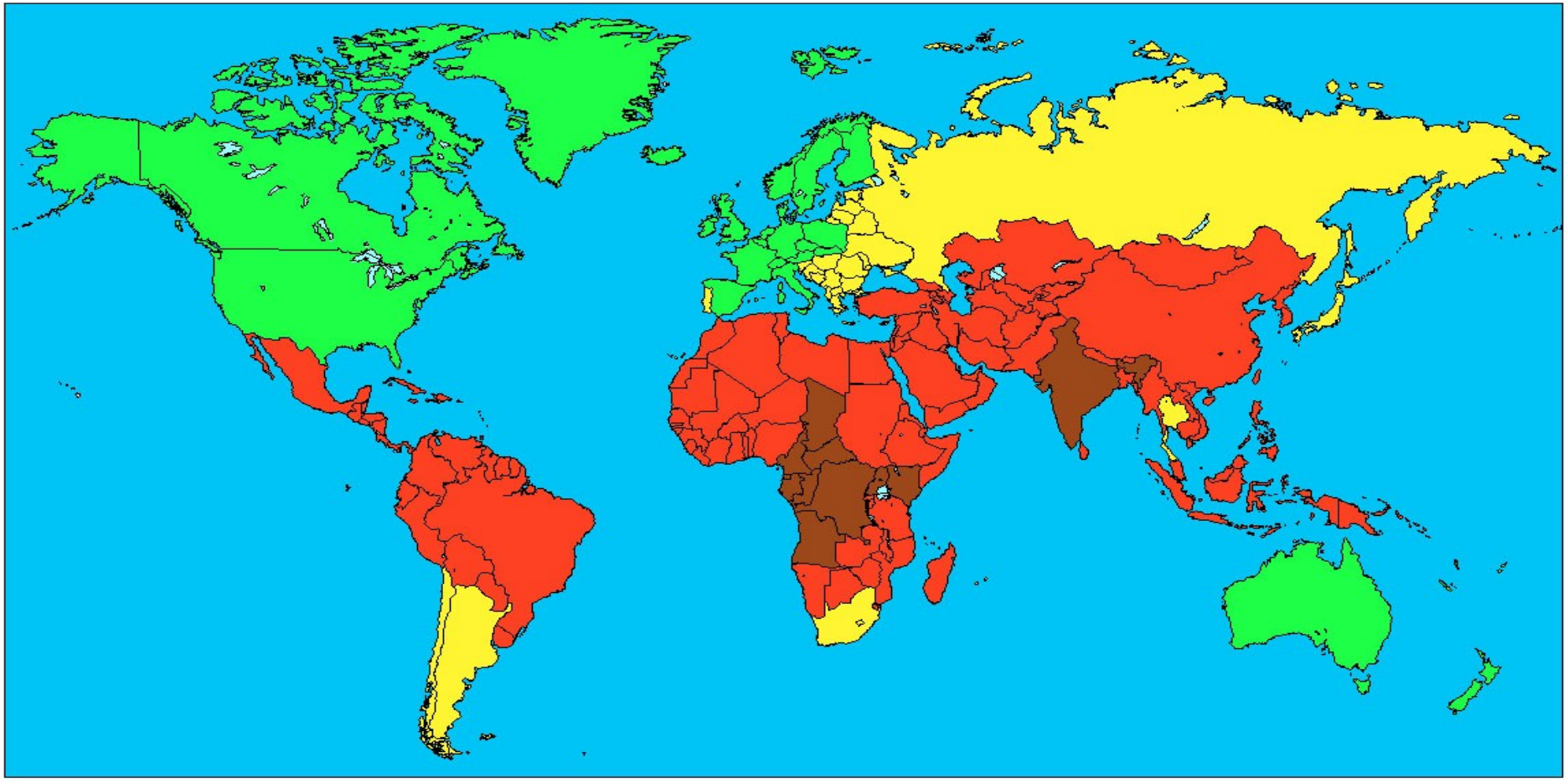
Diarrhea with fever	9-25%
Dysentery	2-8%
Severe diarrhea	
Iraq	21-27%
Afghanistan	13-14%
Vomiting only	5-15%

clinical presentations

operational impact

Job performance	45%
Confined to bedrest	13%
Hospitalized	2%
IV fluids	15-17%
Missed patrol	9-13%
Back-fill needed	12%
Grounded	6-12%
Fecal incontinence	32%

Incidence Rates of Travelers' Diarrhea per 2-week Stay



Epidemiology

- 90% of travelers' diarrhea caused by bacteria
- Most occur between 4-14 days after arrival
- Highest risk area Asia (except for Singapore), Africa (outside South Africa), South and Central America, Mexico
- Stress of travel and hot temperature may make symptoms less tolerable
- Most are self limited, dehydration is main cause of morbidity

Epidemiology in Children

- Major cause of morbidity and mortality
- > 10 illness per child per year
- Asia, Africa, Latin America – 4 million deaths per year
- Up to 50% of childhood deaths

Acute Watery Diarrhea

1). Enterotoxigenic *Escherichia coli* (ETEC)

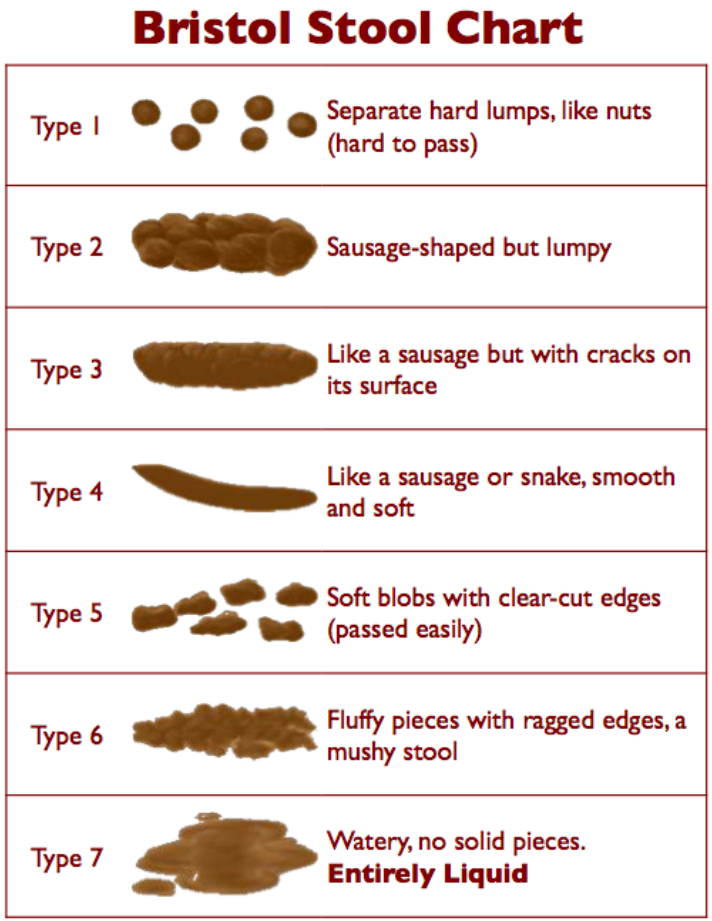
2).Enteroaggregative *Escjerochia coli* (EAEC)

3). *Vibrio cholerae*

4). GI viruses

5). Parasites

6). Food poisoning



Acute Bloody Diarrhea (dysentery)

1). *Shigella* species

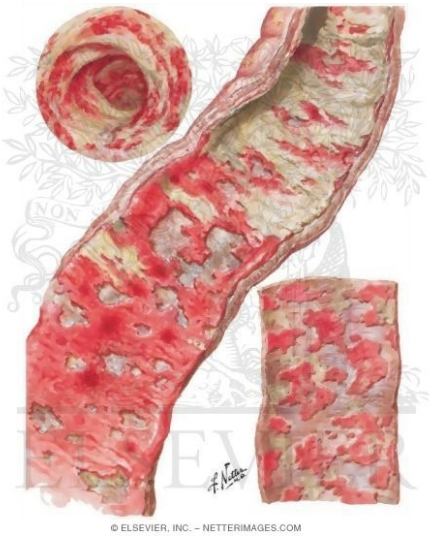
2). Campylobacter species (may be non bloody)

3). Enterohemorrhagic *E.coli* (EH

4). Enteroinvasive *E.coli* (EIEC)

5). Nontyphoidal Salmonella

6). Entamoeba histolytica



Fever

Tenesmus

Mucoid stools

Grossly bloody stools


bacteria

Causative Agents

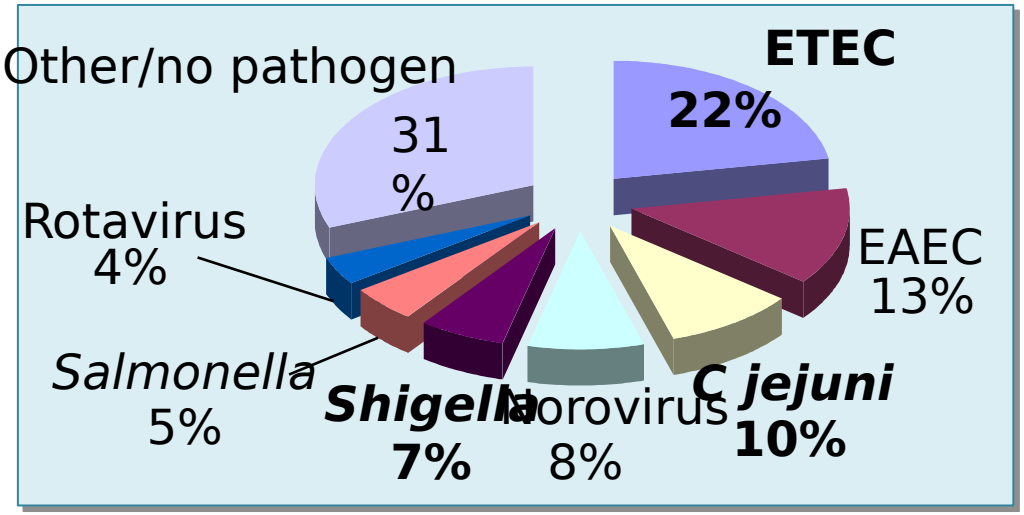

parasites

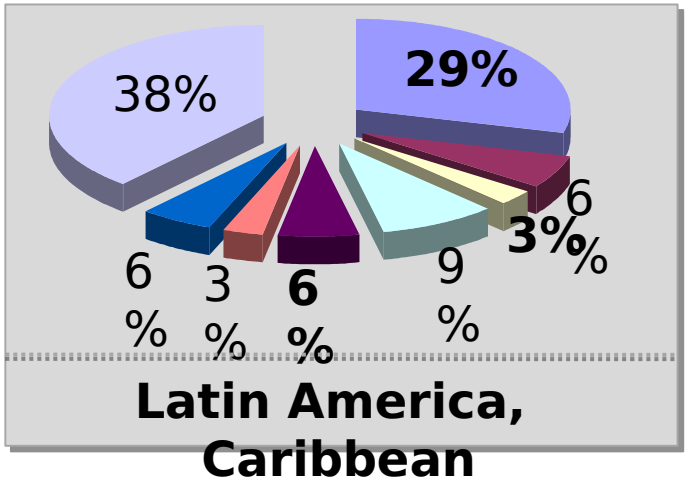
- Bacterial agents (80-90%)
- **Common**
  - Enterotoxigenic *E coli* (ETEC)
  - Enteroaggregative *E coli* (EAEC)
  - *Campylobacter*
  - *Shigella*
  - *Salmonella*
- **Less common**
  - EIEC / EHEC
  - *Vibrio cholerae*

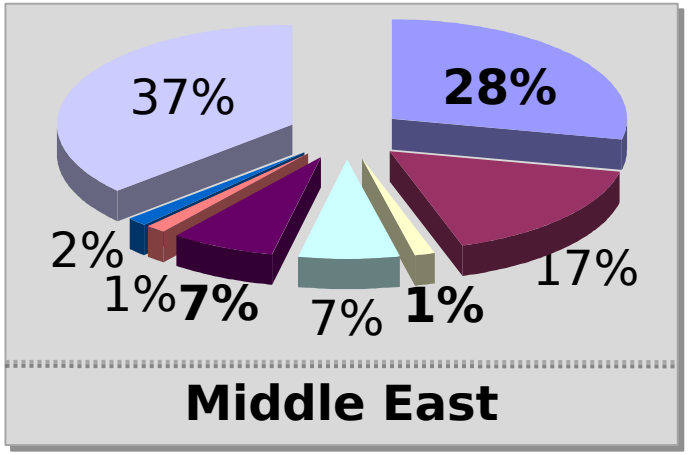
- Viral agents (5-10%)
  - Norovirus
  - Rotavirus
  - Astrovirus
- Parasites (uncommon)
  - *Giardia lamblia*
  - *Cryptosporidium* spp.
  - *Cyclospora cayatanensis*
  - *Entamoeba histolytica*

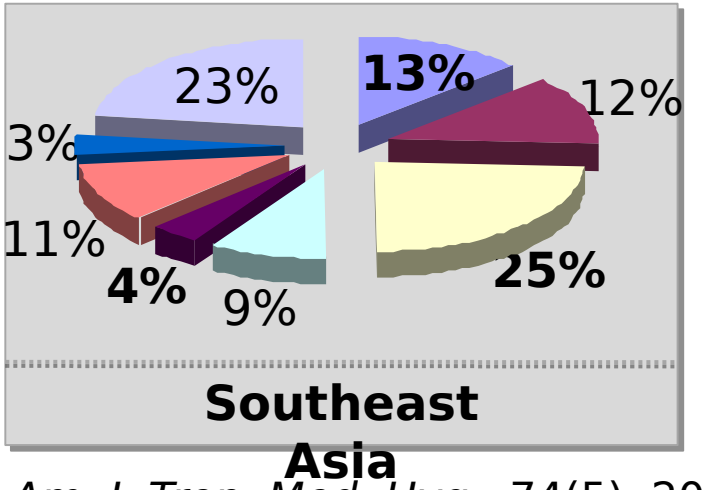

viruses

Etiology of Diarrheal Diseases:
U.S. Military on Deployment



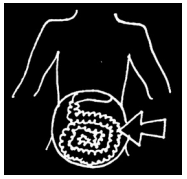






MS Riddle et al. *Am. J. Trop. Med. Hyg.*, 74(5), 2006

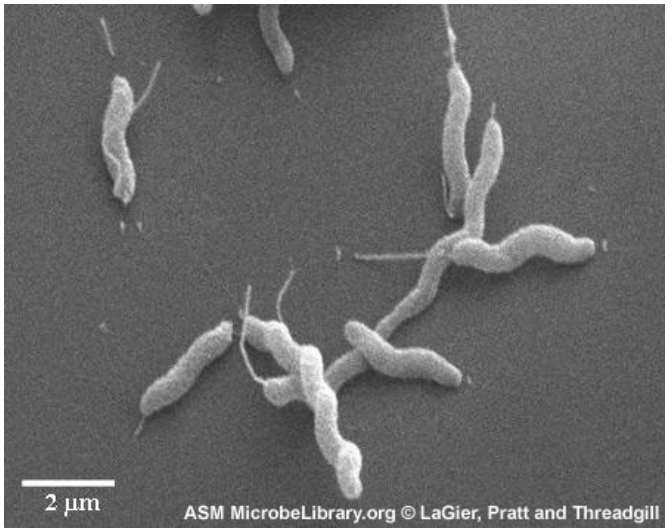
Clinico-pathological Considerations: Acute Travelers' Diarrhea



	Watery diarrhea	Dysentery	Gastroenteritis
Mechanism	Non-inflammatory (enterotoxin)	Inflammatory (invasion or cytotoxin)	Villus blunting (delayed gastric emptying)
Location	Proximal small bowel	Colon or distal small bowel	Small bowel
Usual Pathogens	All causative pathogens; most commonly ETEC, EAEC	*C. jejuni* *Shigella* spp. *Salmonella* (non-typhi) EHEC	Norovirus Rotavirus

Pathogenic Mechanisms

- Inoculum size
  - < 10
    - Norovirus
  - 10-100 organisms
    - *Shigella* species
  - <1000 organisms
    - EHEC
    - *Campylobacter jejuni*
  - > 1,000,000
    - *Vibro cholera*
    - Nontyphoidal *salmonella*
- Adherence
- Toxin Production
- Tissue invasiveness



Risk Factors

- Crowding and poor sanitation
  - Epidemic diarrhea
    - *Shigella dysenteriae*
    - *Vibro cholerae*
- Lower gastric acid secretion
  - Those taking histamine blockers and PPI
  - Those with altered upper GI anatomy
- Immunocompromised host
  - HIV, steroids, autoimmune condition

Types of *E.coli*

- *E. coli* consists of a diverse group of bacteria.
- Pathogenic *E. coli* strains are categorized into pathotypes.
- Six pathotypes are associated with diarrhea

1). Enterotoxigenic E.coli (ETEC)

2). Shiga toxin-prod. *E. coli* (STEC) / Enterohemorrhagic *E. coli* (EHEC).

3). Enteroaggregative *E. coli* (EAEC)

4). Enteroinvasive *E. coli* (EIEC)

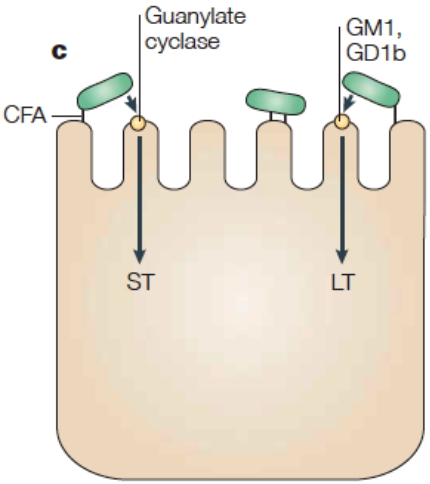
5). Enteropathogenic *E. coli* (EPEC)

6). Diffusely adherent *E. coli* (DAEC)

Enterotoxigenic *E. coli* (ETEC): Features

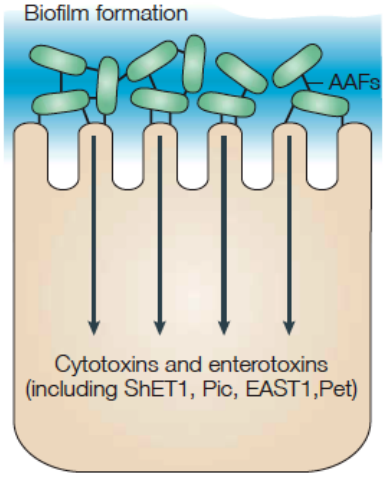
Transmission	foodborne (food, water)
inoculum size	High (≥ $5x10^6$ organisms)
populations at risk	infants, LDC; travelers to endemic regions
Estimated no. cases annually	200 million worldwide; > 500,000 under five death per year
typical clinical syndrome	watery diarrhea; dehydration in moderate-severe disease
phenotypic diversity	2 enterotoxins; > 20 fimbrial types
sequelae	physical and cognitive retardation; malnutrition

Escherichia coli Common in Travelers



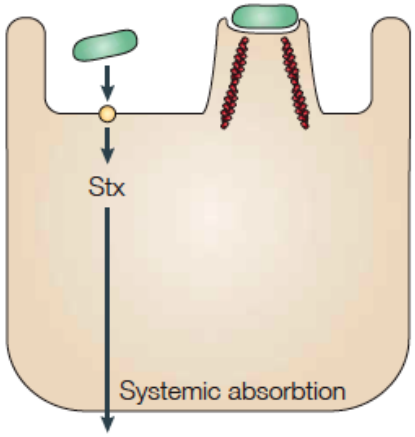
ETEC

- Fimbrial colonization factors mediate enterocyte adherence
- Elaboration of secretory heat-labile (LT), heat-stable (ST) enterotoxins



EAEC

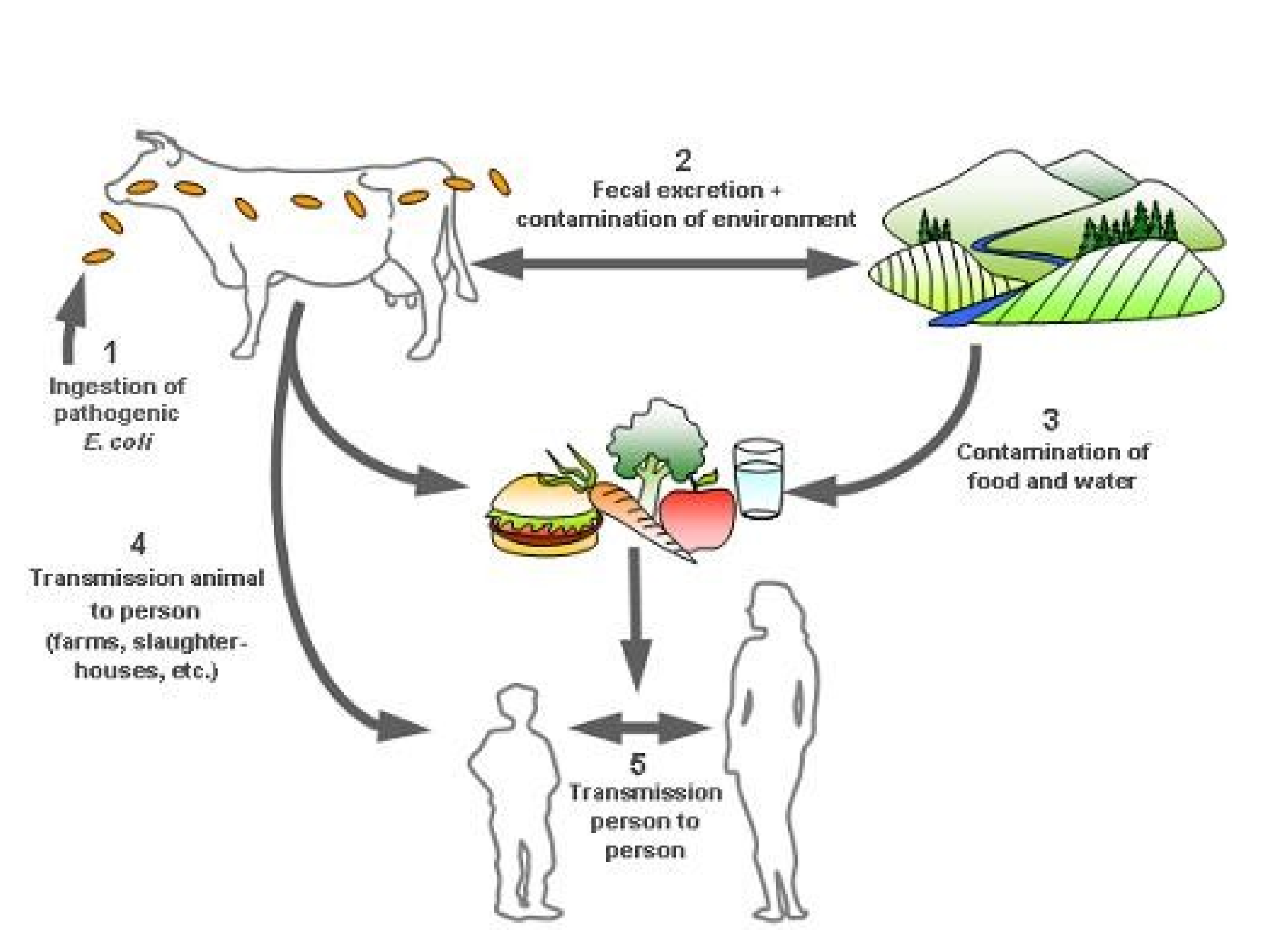
- Enterocyte adherence and **biofilm formation**
- Elaboration of secretory enterotoxins and cytotoxins



STEC / EHEC

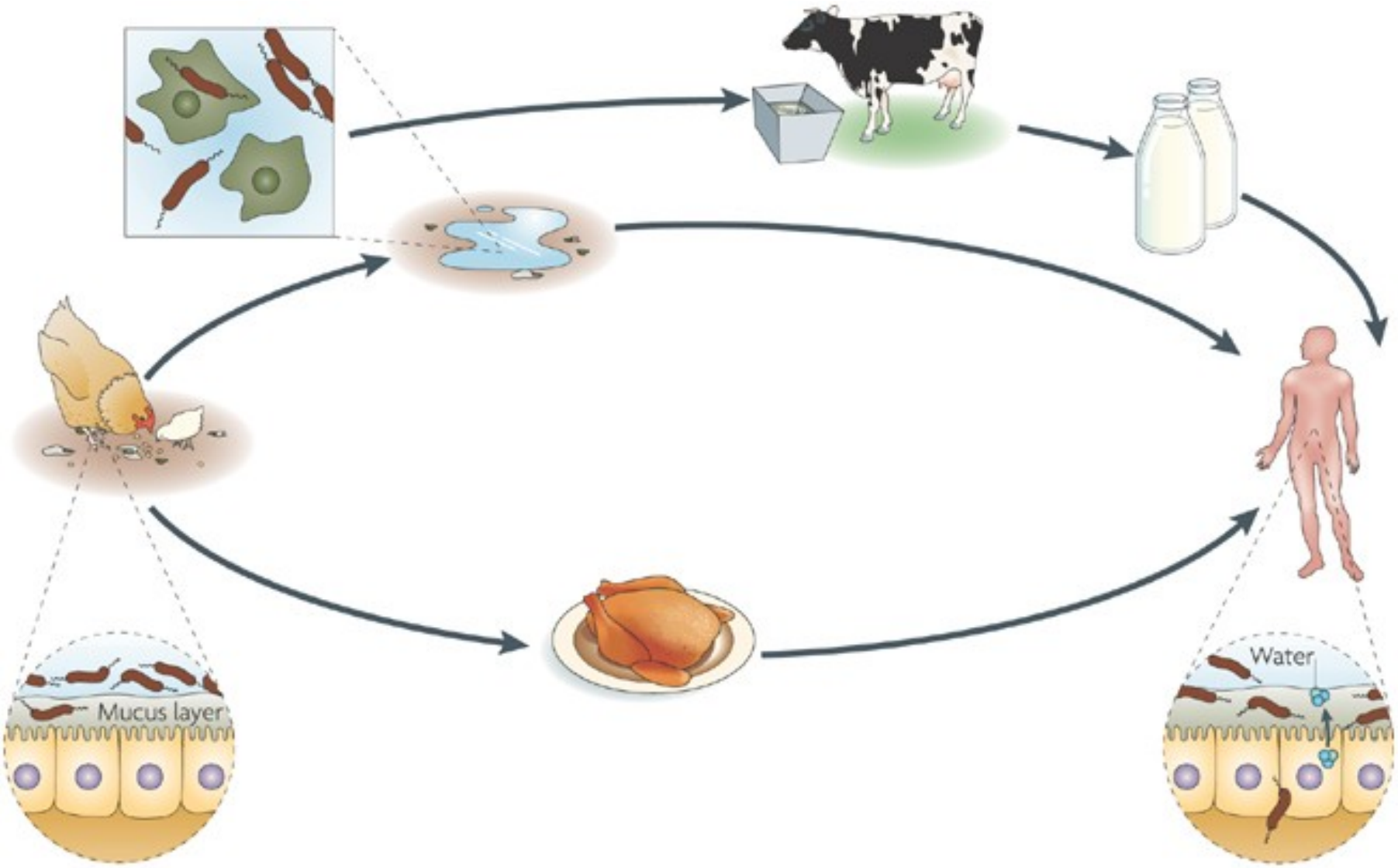
- Induction of **attaching and effacing** (AE) lesions in the colonic epithelium
- Elaboration and absorption of **Shiga toxin** (STx)

adapted from Kaper JB et al *Nat Rev Microbiol* 200


1
Ingestion of pathogenic *E. coli*
2
Fecal excretion + contamination of environment
3
Contamination of food and water
4
Transmission animal to person (farms, slaughter-houses, etc.)
5
Transmission person to person

Campylobacter jejuni: Features

Transmission	foodborne (food, water)
inoculum size	low (≥ $5x10^2$ organisms)
populations at risk	infants, LDC; travelers to hyperendemic regions; young people, HDC
geographic 'hotspots'	SE Asia, North Africa (Morocco)
typical clinical syndrome	acute inflammatory enteritis
serotypic diversity	multiple (108 Lior, 47 Penner serotypes)
sequelae	reactive arthritis; Guillain-Barré syndrome; irritable bowel syndrome


Mucus layer
Water

Shigellosis: Features

transmission	**person-to-person**; foodborne (food, water)
inoculum size	low (10-200 organisms)
reservoirs	**humans** only
populations at high risk	toddlers living in and travelers to LDC; crowding, poor sanitation (e.g., day care, institutions)
serotypic diversity	Over 50 different serotypes (determinant, LPS)
key pathogenic processes	invasion, spread, inflammatory response; cytotoxicity (*S. dysenteriae* type 1, Shiga toxin)
typical clinical syndrome	**dysentery** (most commonly)
natural immunity	Medium-term, serotype-specific immunity
sequelae	Reiter's syndrome; reactive arthropathy; hemolytic uremic syndrome

LDC, less developed countries

Differential Morbidity Associated with Major Bacterial Pathogens of Travelers' Diarrhea

Pathogen profile	ETEC	*C jejuni*	*Shigella*
Global prevalence (%)	22 (17-28)	10 (5-15)	7 (3-10)
Illness duration w/o treatment (mean, d)	3.6	8.0	7.1
Probability of causing incapacitation (%)	21-27	47	56-92
Illness duration after treatment (mean, d)	1.0	2.5	1.2

Salmonella

- Typhoidal Salmonella
  - *S. typhi* or *S. paratyphi*
  - Typhoid or Enteric fever
  - Colonized humans, fecal-oral transmission
  - Systemic illness with very little or no diarrhea (small bowel disease)

- Non-typhoidal Salmonella
  - Several species
  - Not common cause of traveler's diarrhe
  - Animal or human fecal material
    - Poultry, pets
  - Invasive, bloody stools

Virbrio cholerae
Toxigenic serogroups 01 or 0139

- Free living organisms in brackish water
- Epidemics throughout human history
  - Spreads quickly
- Acute watery diarrhea
- Food or water contaminated with human fecal material
- Cholera enterotoxin
  - Stimulates secretory mechanism of intestinal mucosa
- 1/5 infected will have severe disease, diagnose by culture
- Rehydration is key
- Tetracyclines, doxycycline, ciprofloxacin reduces illness
- Oral vaccine available (not in U.S)
  - Incomplete, short protection

Broad (Broadwick) Street Pump

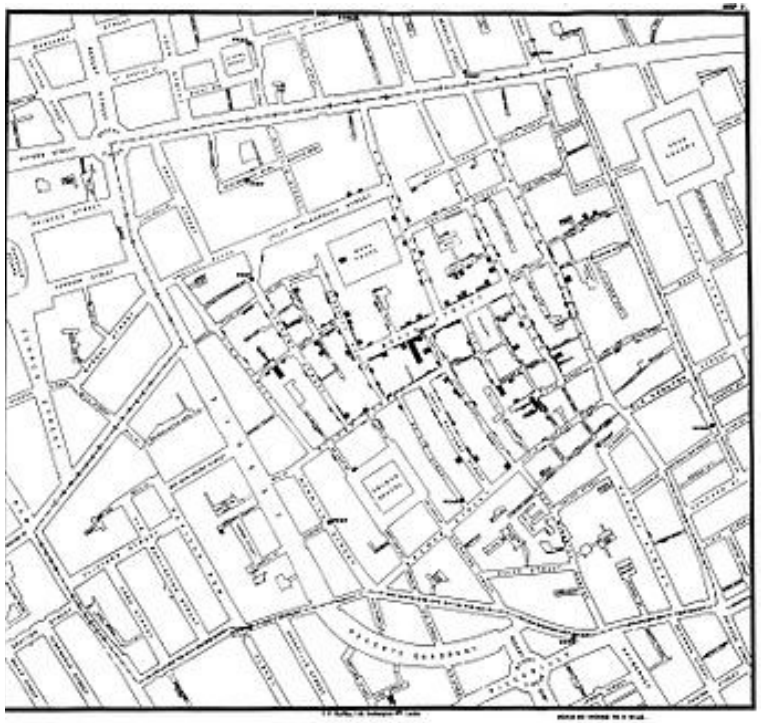
Medical Societies.

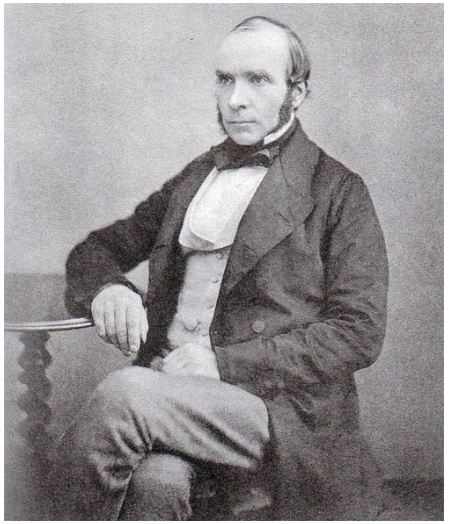
MEDICAL SOCIETY OF LONDON.

Mr. Headland, President.

Saturday, October 14th, 1854.

Dr. Snow considered that the cholera poison acted upon the alimentary canal, and not on the blood or nervous system. In every case which he had seen, the evacuations had been sufficient to account for the collapse, without reference to any other cause. There was no poison in the blood in a case of cholera; in the consecutive fever, as it was called, the blood became poisoned from urea getting into the circulation in consequence of the kidneys not acting, but not from any poison having been present from the beginning. There was nothing in the atmosphere to account for the spread of cholera, which he believed was spread from person to person; and that in all cases it could be traced in this manner. If atmospheric, why did it attack one or two persons only in a locality, and these having direct communication with each other? Such cases he had seen at Sydenham, where there had been only two instances of the disease. The first case in the outbreak of 1849 had occurred to a sailor in Bermondsey; the second affected person was the successor to the sailor in the room in which he died. He thought he had collected evidence enough to show that in all cases cholera was propagated by swallowing some portion of the evacuations of an affected person. These, as was well known, flowed into the bed, &c., and persons attending on the sick might easily take the poison unawares. With respect to the class of persons affected by the disease, he believed that the very poor and vagabonds suffered less, in proportion, than decent, respectable persons. He regarded the cholera and diarrhœa, as lately prevalent, to be the same disease in different degrees of intensity. We observed the same difference in scarlatina and other diseases.



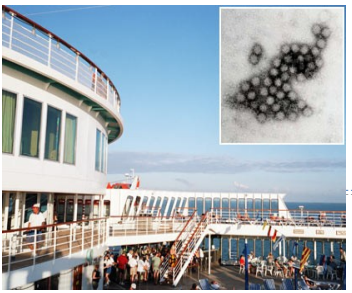


Dr. John Snow

Comparison of clinical feature of epidemic dysentery and cholera

	Epidemic Dysentery	Cholera
Causative organism	*Shigella dysenteriae* type 1	*Vibrio cholerae* O1 (*Vibrio cholerae* O139)
Infective dose	10 to 100 organisms	1000 to 1,000,000 organisms
Clinical features	Bloody diarrhea Abdominal cramps Fever Rectal pain	Watery diarrhea Dehydration Vomiting
Complications	Seizures Rectal prolapse Hemolytic-uremic syndrome Sepsis	Severe hypovolemia/shock Electrolyte abnormalities
Treatment	Antibiotics	Rehydration
Transmission	Food and water Person-to-person	Food and water
Case fatality rate	10 to 20 percent (untreated) 5 percent (treated)	40 percent (untreated) <1 percent (treated)

Regina C LaRocque, MD, MPH, and Mark Pietroni, MA, MBBChir, FRCP, DTM&H.



Noroviruses: Features

transmission	foodborne (food, water); person-to-person (crowdi
inoculum	low (as few as 10 viral particles)
reservoirs	**humans** only; hardy virus, persists on fomites
populations at high risk	All age groups; outbreak potential in semi-closed populations – military populations, including ships
genotypic diversity	3 genogroups, and ≥ 25 genotypes
key pathogenic processes	Limited to small intestine, broadening/blunting of proximal intestinal villi; transient malabsorption
typical clinical syndrome	Sudden onset of vomiting and non-inflammatory diarrhea; duration typically ≤72 hours
natural immunity	Short-term homologous immunity; possible long-term immunity with repeated exposure
sequelae	No evidence of serious long-term sequelae

Acute Water Diarrhea

Watery stools of <14 days duration, with no visible blood constitutes acute watery diarrhea.

(A) Green watery stool. Green colored stool, often seen in rotavirus gastroenteritis.

(B) Rice water stool. White colored stool characteristic of severe cholera.

Clinical and Diagnostic Evaluation

- Assess for dehydration
  - Mild (3-5%): dry mouth, decreased sweat and urine output
  - Moderate (6-9%): orthostasis, skin tenting, sunken eyes
  - Severe (>10%): hypotension, tachycardia, confusion, shock
- Consider setting of illness
  - Host factors
  - Environment, geographic region
  - Pathogen
- Define the clinical syndrome
  - Watery diarrhea
  - Dysentery
  - Gastroenteritis with recurrent vomiting
  - Persistent diarrhea

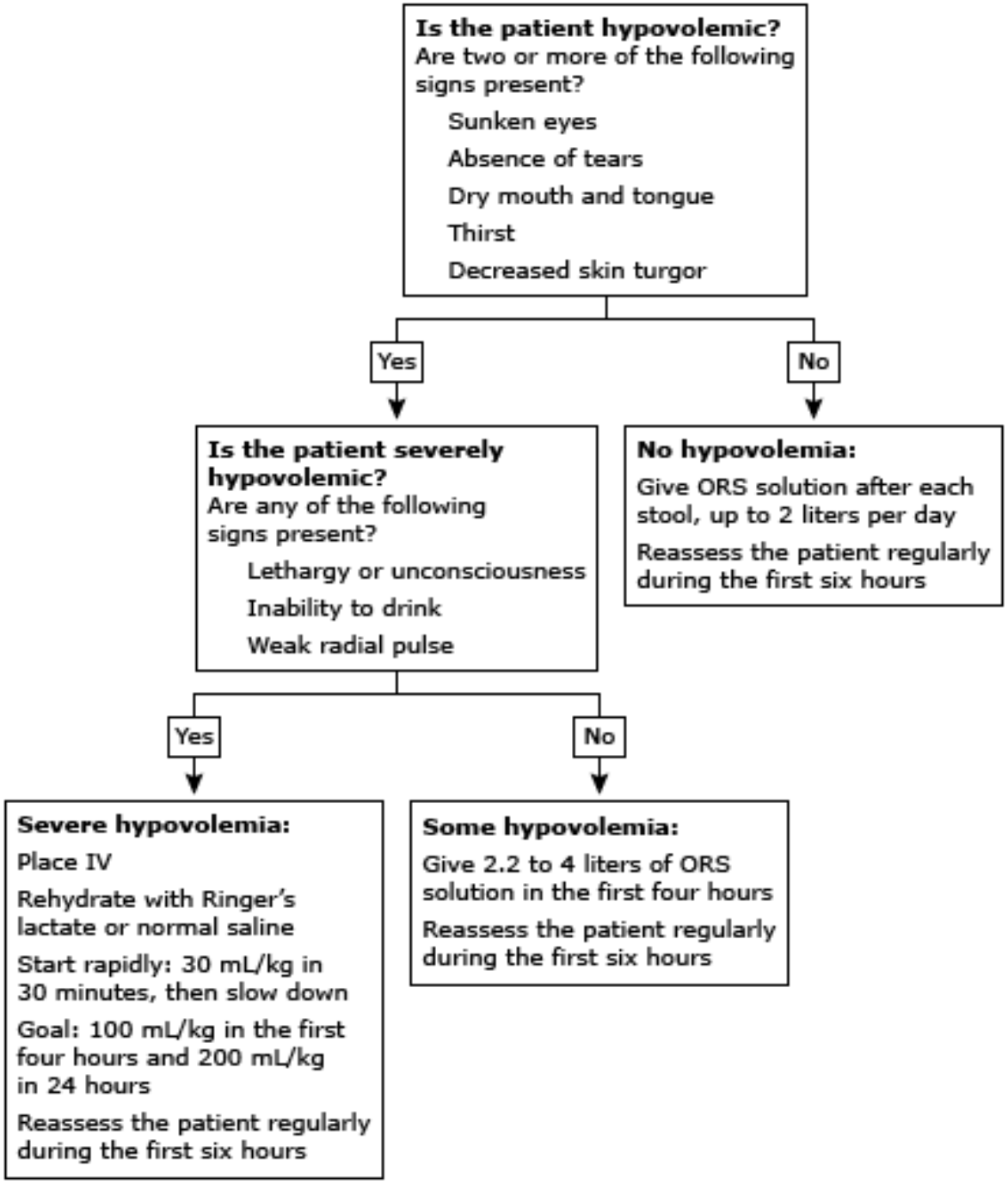
Considerations for Laboratory Work-up

- With military deployments, available laboratory capabilities may be austere
- Several common pathogens are not detectable with routine laboratory diagnostic tests
  - Diarrheagenic *E. coli* (ETEC, EAEC, EIEC)
  - Norovirus
- **Differentiate inflammatory vs. non-inflammatory diarrhea**
  - Clinical indicators of inflammatory disease include fever, tenesmus, visible blood in stool
  - Gross and microscopic examination of stool for blood and fecal leucocytes

Considerations for Laboratory Work-up (level III)

- Stool culture: clinical indications
  - Severe diarrhea (≥ 6 loose/liquid stools/24 hrs, incapacitating illness)
  - Febrile enteritis and/or dysentery
  - Persistent diarrhea (≥ 14 days duration)
  - Bloody diarrhea (at risk for Shigella, STEC)
  - Inflammatory enteritis (by stool diagnostics)

- Stool parasitology: clinical indications
  - Persistent diarrhea (≥ 14 days duration)
  - Diarrhea in traveler returning from known high risk region


Is the patient hypovolemic?
Are two or more of the following signs present?
Sunken eyes
Absence of tears
Dry mouth and tongue
Thirst
Decreased skin turgor
Yes
No
No hypovolemia:
Give ORS solution after each stool, up to 2 liters per day
Reassess the patient regularly during the first six hours
Is the patient severely hypovolemic?
Are any of the following signs present?
Lethargy or unconsciousness
Inability to drink
Weak radial pulse
Yes
No
Severe hypovolemia:
Place IV
Rehydrate with Ringer's lactate or normal saline
Start rapidly: 30 mL/kg in 30 minutes, then slow down
Goal: 100 mL/kg in the first four hours and 200 mL/kg in 24 hours
Reassess the patient regularly during the first six hours
Some hypovolemia:
Give 2.2 to 4 liters of ORS solution in the first four hours
Reassess the patient regularly during the first six hours

Therapeutics: Water and Electrolyte Replacement

- Cornerstone of diarrhea treatment
- Military settings, insensible fluid losses increased with high ambient temperature, intense physical activity
- Oral rehydration
  - Physiological principle: Integrity of coupled transport of Na+ (plus H_2O and other electrolytes) with glucose or amino acids
  - Effective in majority of patients
- Intravenous rehydration
  - Severe dehydration
  - Altered sensorium
  - Intractable vomiting

Oral Rehydration Therapy

- Mild dehydration
  - Potable water or appropriate ORS
- Moderate-severe disease
  - ORS (Oral Hydration Salts)

	CHO g/L	Na mmol/L	CHO:Na	K mmol/L	OSM mOsm/kg
Rehydration Formulas					
WHO ORS	**13.5**	**75**	**1.2**	**20**	**245**
Pedialyte	25	45	3.1	20	250
Sports Drinks					
Gatorade	45	20	13	3	330
Powerade	60-80	~10	~6	~3	346-391
Other fluids					
Red Bull	108	35	~3	0	601
Apple Juice	690	3	230	32	694-773
Chicken Broth	0	250	-	8	500

Non-Antibiotic Therapy

- Consider with mild diarrhea for symptomatic relief
- Loperamide (imodium): antimotility agent of choice
  - Slows down peristalsis, intestinal transit
  - Increased fluid and salt absorption
  - 4 mg by mouth, then 2 mg after each liquid movement (up to 16 mg per day)
  - Okay to use for non-bloody, non-febrile diarrhea.
- Bismuth subsalicylate (Pepto Bismol)
  - Reduces number of passes stools
  - Does not limit duration of disease
  - 525 mg (2 tabs) every 30 min for 8 doses
  - Contraindicated in persons on salicylates, warfarin
  - Can interfere with doxycycline absorption (malaria prophylaxis)

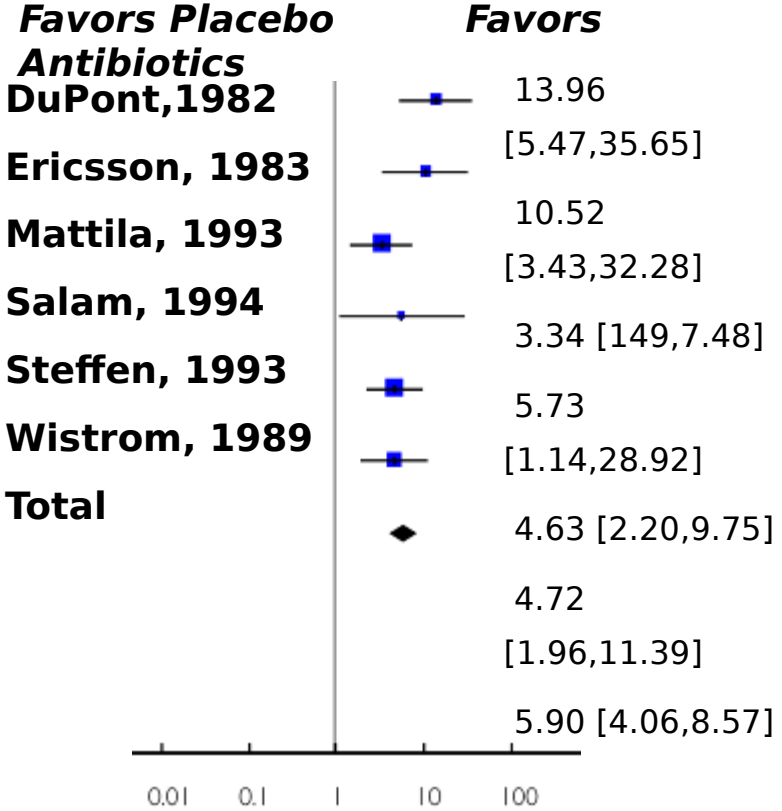
Empiric Antibiotic Therapy

- Indicated for patients with moderate to severe diarrhea/dysentery
- Combination of antibiotic PLUS loperamide leads to rapid resolution of illness
- Re-evaluate patient if no improvement after 1 wk

Antibiotic (po)	Dosage (adult)	Considerations
Fluoroquinolones		
Norfloxacin	800 mg once or 400 mg bid	Re-evaluate 12-24 h after single dose. Continue for up to 3 d if diarrhea not resolved
Ciprofloxacin	750 mg once or 500 mg bid	
Ofloxacin	400 mg once or 200 mg bid	
Levofloxacin	500 mg once or 500 qd	
Azithromycin	1000 mg once or 500 mg bid x 3 d	Use when *C. jejuni* suspected
Rifaximin	200 mg tid	Effective for non-invasive *E coli*

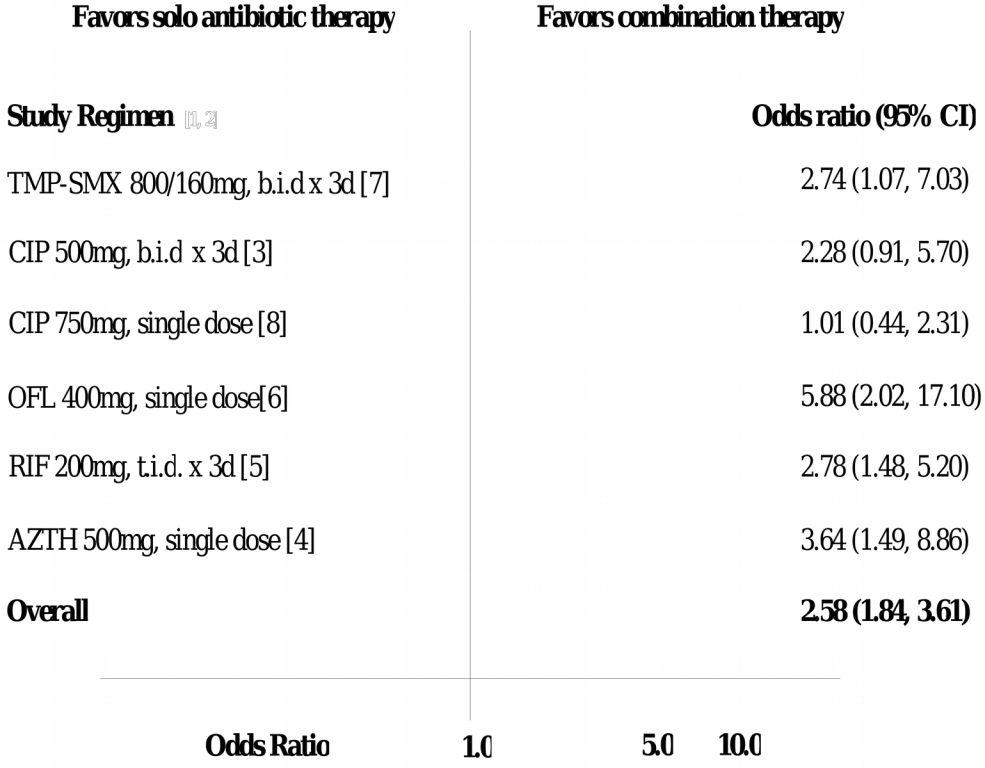
Effectiveness of Antibiotics, and Additive Effect of Loperamide)

Placebo vs antibiotics alone (outcome: cure at 72 hours) Bruyn G et al Cochrane Collab 2004



TLUS = 24 – 36 hours

Antibiotics alone or plus **loperamide** (outcome: cure at 24 hours) Riddle MS et al, CID 2008



TLUS ~ 12 hours

Increasing Fluoroquinolone Resistance among *Campylobacter* in Travele

Region	1994-2000 No. isolates	No. resistant isolates	Resistance rate (%)	2001-2006 No. isolates	No. resistant isolates	Resistance rate (%)
Africa	162	22	13.6	114	36	31.6
Asia	208	74	35.6	95	67	70.5
Caribbean, Central & So. America	36	10	27.8	33	20	60.6

Use Azithromycin in SE ASIA, 1000 mg x 1 may be enough

- Study site: Travel clinic, Antwerp, Belgium
- Erythromycin resistance showed modest increase over same period to 8.6% resistance in 2006

Vlieghe ER et al, *J Travel Med* 2008;15:419-25

Pediatr Nephrol (2008) 23:1425–1431
DOI 10.1007/s00467-008-0820-3

EDUCATIONAL REVIEW

Enterohaemorrhagic *Escherichia coli* and *Shigella dysenteriae* type 1-induced haemolytic uraemic syndrome

C. Mark Taylor

Abstract Haemolytic uraemic syndrome (HUS) can be classified according to the aetiology of the different disorders from which it is composed. The most prevalent form is that induced by shigatoxin producing *Escherichia coli* (STEC) and, in some tropical regions, by *Shigella dysenteriae* type 1. STEC cause a zoonosis, are widely distributed in nature, enter the food chain in different ways, and show regional differences. Not all STEC are human pathogens. Enterohaemorrhagic *E. coli* usually cause attachment and effacing lesions in the intestine. This is not essential, but production of a shigatoxin (Stx) is. Because Stx are encoded by a bacteriophage, this property is transferable to naïve strains. Laboratory methods have improved by identifying STEC either via the toxin or its bacteriophage. *Shigella dysenteriae* type 1 produces shigatoxin, identical to Stx-1, but also has entero-invasive properties that enterohaemorrhagic *Escherichia coli* (EHEC) do not. Shigella patients risk bacteremia and benefit from early antibiotic treatment, unlike those with EHEC.

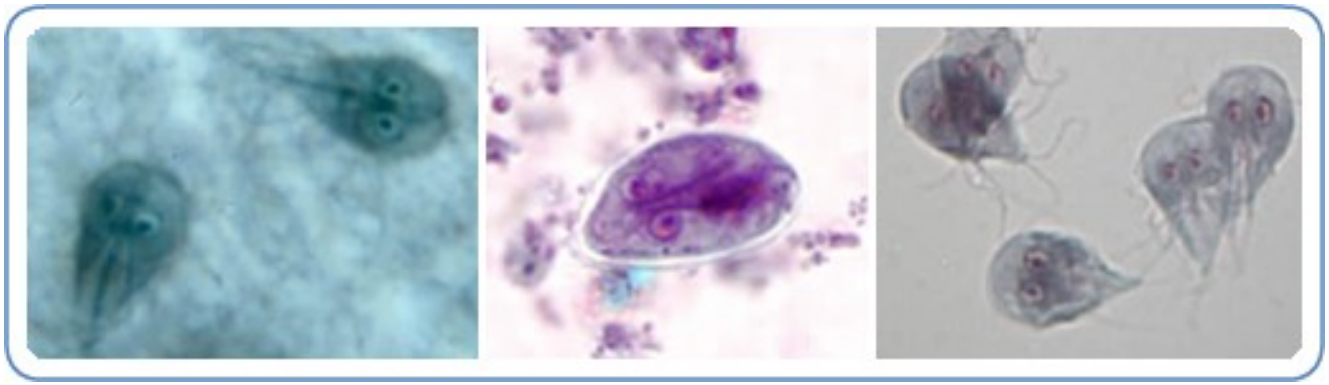
Complications of Bacterial Diarrhea

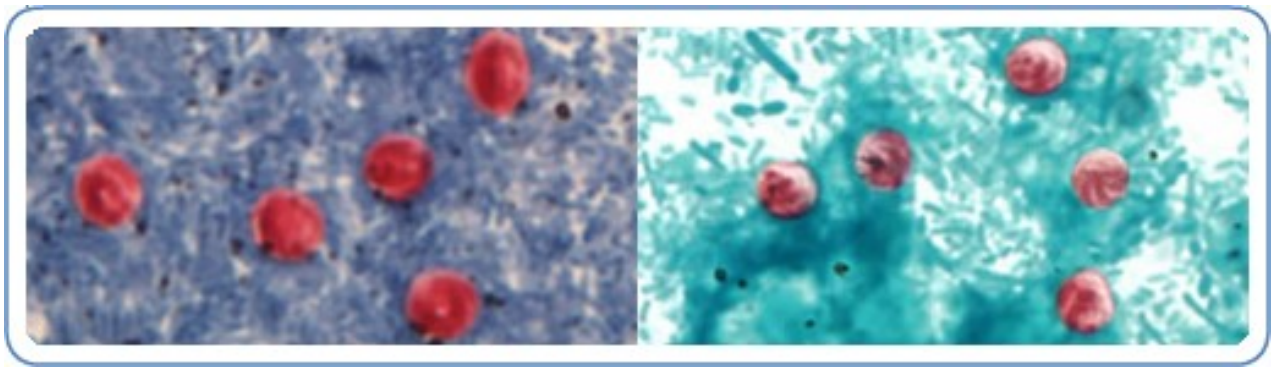
Complication	Associated Bacterial Agents	Clinical Considerations
Dehydration	Any bacterial pathogen	Most important complication of watery diarrhea
Bacteremia	*Salmonella* spp., *C. fetus*	Certain conditions predispose to systemic *Salmonella* infection
Hemolytic-uremic syndrome (HUS)	STEC, *S. dysenteriae* type 1	Pathogenesis due to shiga toxin absorption and damage
Guillain-Barré syndrome	*Campylobacter jejuni*	40% cases of GBS caused by *C. jejuni;* molecular mimicry LOS
Reactive arthritis	*C. jejuni, Salmonella, S. flexneri*	Occurs in 2.1 per 100 000 *Campylobacter* infections
Irritable bowel syndrome	Most bacterial pathogens	≤ 10% incidence following bacterial enteric infection

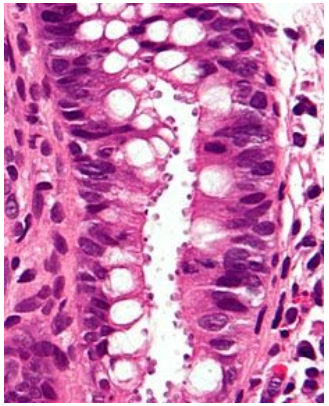
Antibiotic associated GI problems

- Any antibiotic can cause upset stomach, loose stools
- *Clostridium difficile* infection happens when normal bacteria are killed
- *C.difficle* patients have high fever, highly elevated WBC's, large volume smelly stools, and appear sick (not always).
- *C.difficile* may be 'community onset'
- Treatment is metronidazole

Intestinal parasites

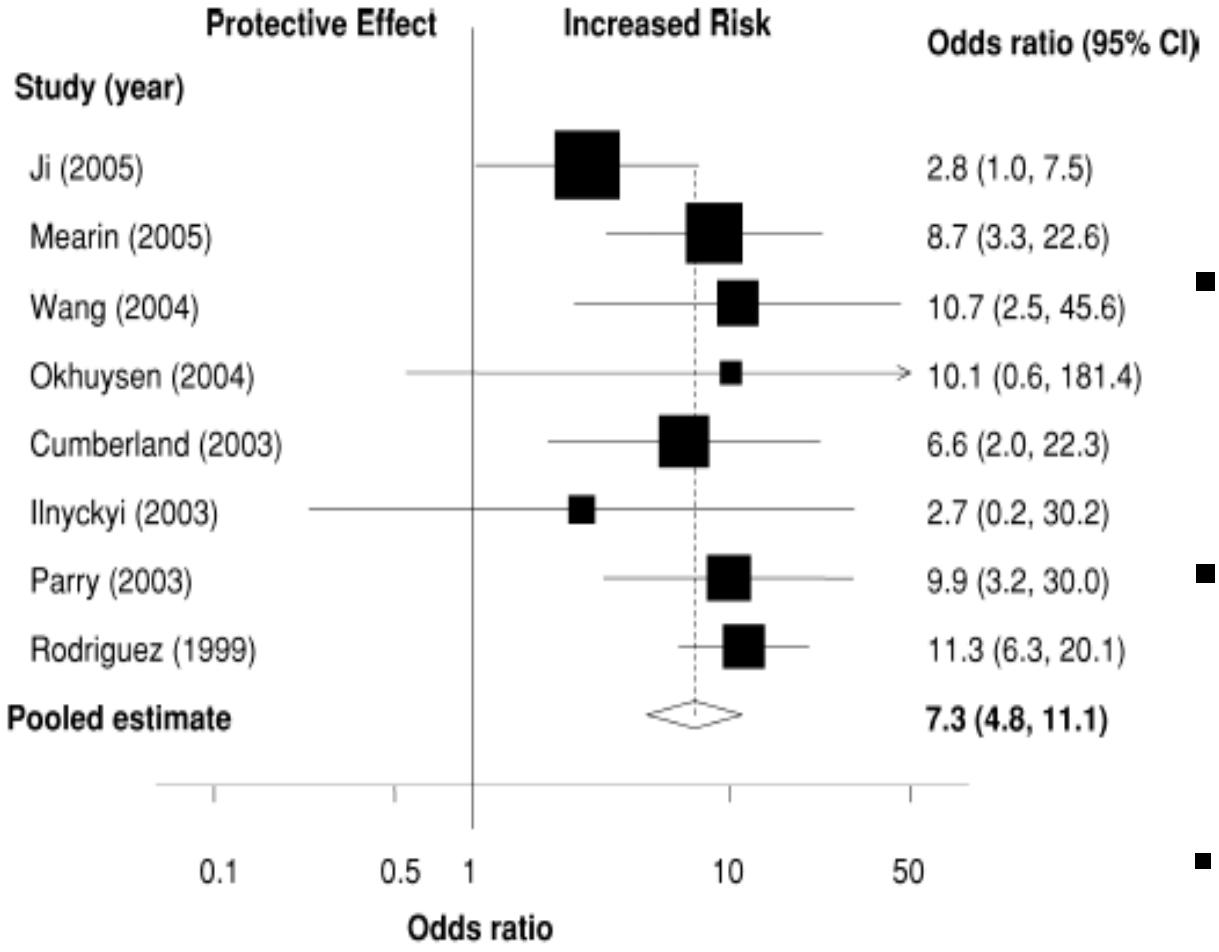






CDC Image

Postinfectious Irritable Bowel Syndrome (PI-IBS)



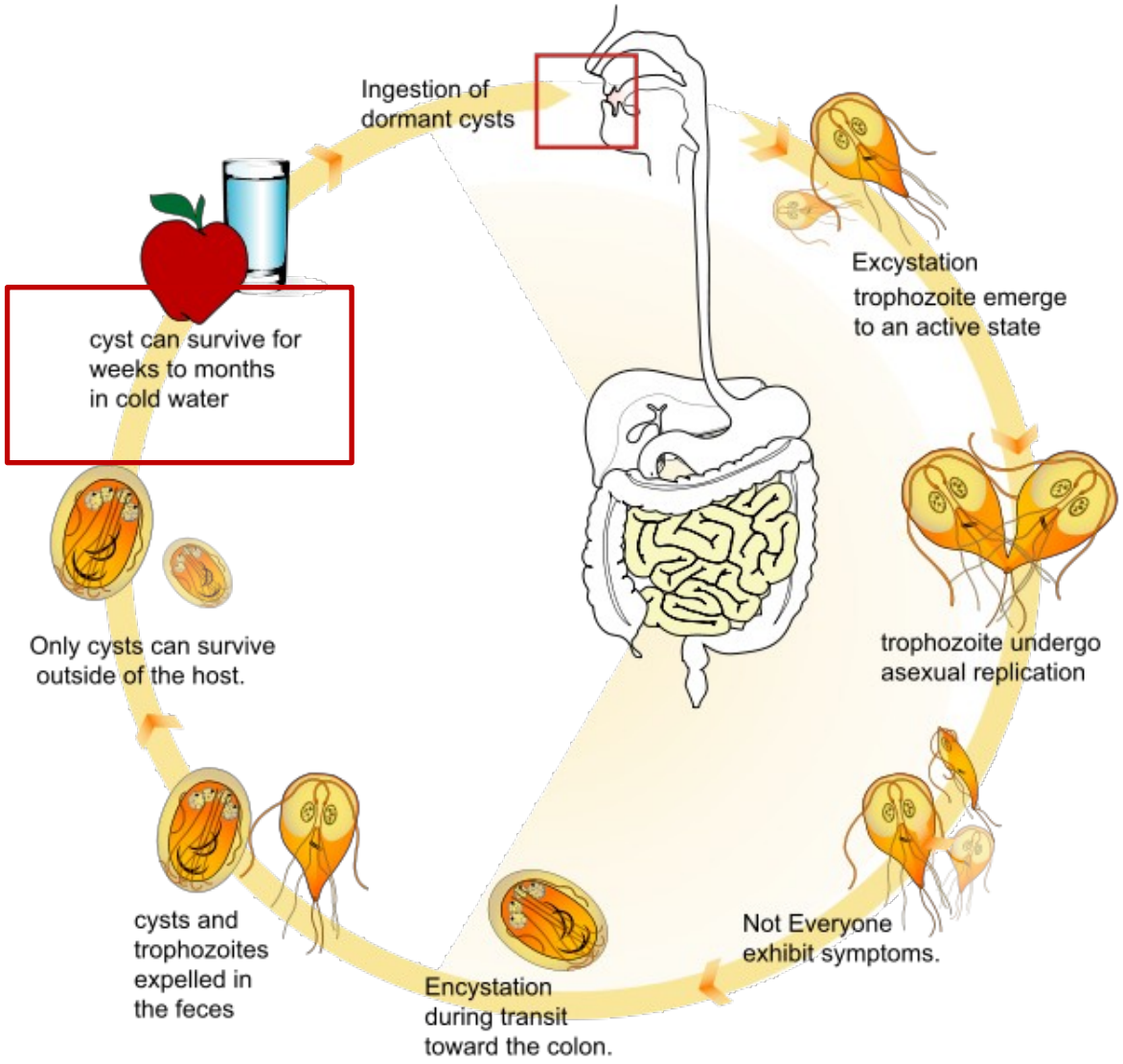
Halvorson *et al*, Am J Gastroenterol. *2006; 101:1894-9*

- First described among British Forces during WWII **(Stewart. *Br Med J* 1950; 1(4650):405–9)**
- Approx. 1 in 12 people develop PI-IBS after infectious diarrhea
- Higher risk associated with prolonged illness and invasive pathogens
- Onset usually occurs within 6 months after infection
- Can persists 5-6

Persistent Travelers' Diarrhea

- Travelers' diarrhea is often self-limited, resolving in the majority of cases after several days
- Illness lasting >1 week: 10% of cases
- Illness lasting >1 month: 2% of cases
- Etiological considerations with persistent diarrhea
  - EAEC (occasionally, *Campylobacter*, *Salmonella*)
  - Parasitic diarrhea
    - *Giardia lamblia*
    - *Cryptosporidium parvum*
    - *Cyclospora cayatanensis*

Giardiasis: *Life Cycle*

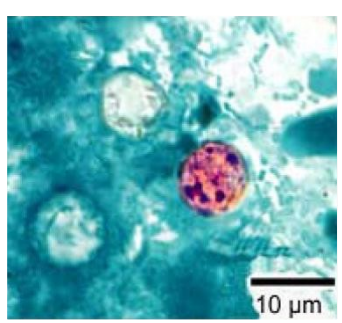


Giardiasis: Features

transmission	contaminated water; infected food handlers
inoculum size	low (as few as 10-25 cysts)
reservoirs	Humans and other mammals
populations at high risk	backpackers; young children LDC; higher risk with travel to Russia, Mexico, SE Asia, South America
antigenic variation	on-off switch of variant specific surface proteins (V
key pathogenic processes	Attachment to intestinal epithelium via ventral disc; flagellar motility; VSP switching evades IgA
typical clinical syndrome	watery diarrhea; **epigastric abdominal pain, bloating**, malabsorption, nausea, weight loss
treatment	Self-limited. Metronidazole, tinidazole
sequelae	Functional gastrointestinal disorders (IBS)

Cryptosporidium: Features

transmission	contaminated water and food; person-to-person
inoculum size	low (as few as 10 oocysts)
reservoirs	humans and other mammals (including livestock)
populations at high risk	HIV/AIDS; urban populations, municipal water contamination; children in LDC; travelers
species diversity	majority of human cases due to *C. hominis, C. parv*
key pathogenic processes	Localizes in parasitophorous vacuoles in intestinal epithelium; distal small intestine; villous atrophy
typical clinical syndrome	watery diarrhea, abdominal cramps, vomiting, mild fever, and loss of appetite
treatment	Self limited. None great, nitazoxanide
sequelae	intractable diarrhea in immunocompromised patients



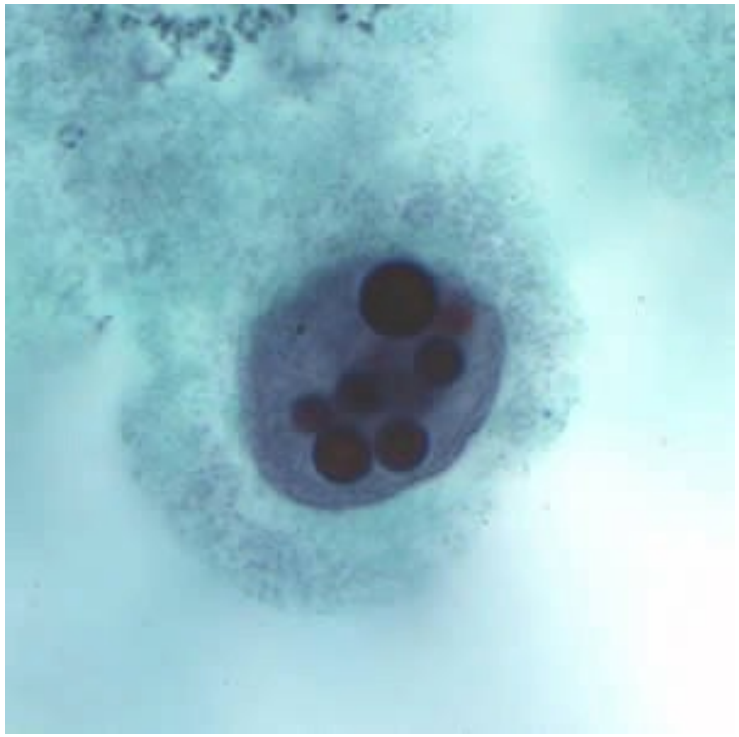
Cyclosporiasis: Features

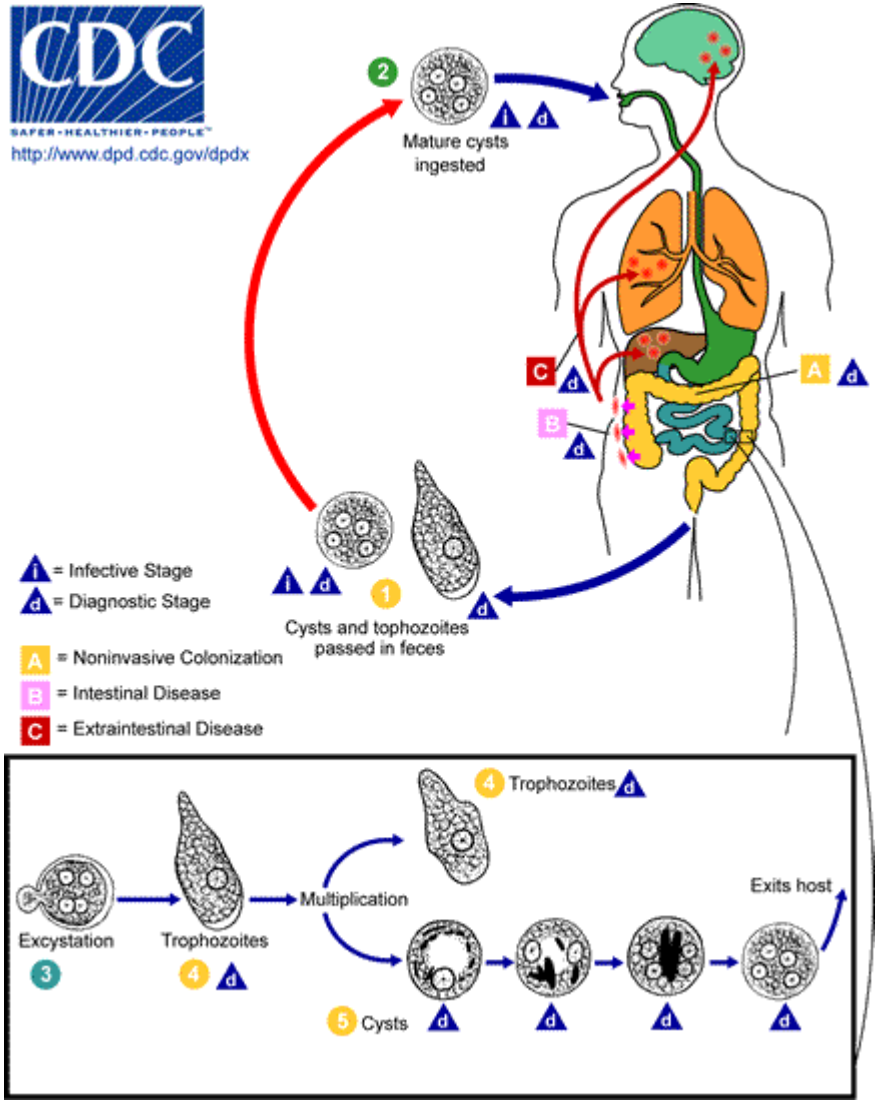
transmission	contaminated food and water; no person-to-person
inoculum size	undefined
reservoirs	environmental; may be host species-specific types
populations at high risk	young children in LDC; travelers (especially Peru, Nepal, Haiti, Guatemala (*); immunocompromised
species diversity	*C. cayatanensis* found only in humans
key pathogenic processes	not well understood; localizes to small intestinal epithelium, partial villous atrophy, crypt hyperplasia
typical clinical syndrome	persistent diarrhea, anorexia, nausea/vomiting, abd cramps, flatulence, low grade fever, weight loss
treatment	Self-limited, Trimethoprim-sulfamethoxazole (TMP/SMX)
sequelae	Chronic diarrhea in immunocompromised patients

Amebiasis

- Protozoan parasite *Entamoeba histolytica*
- Not common traveler's diarrhea pathogen
- Longer stays in tropical endemic area
- Fecal oral spread
- Most infections (90%) have no symptoms or mild diarrhea
- Amebic dysentery is severe infection
  - Fever, bloody stools
  - Look for trophozoite in stool
  - May be confused with non-pathogenic species
- Liver abscess and systemic infection
- Treatment: iodoquinol, paromomycin, metronidazole

Entamoeba histolytica





CDC

COMPENDIUM OF ACUTE FOODBORNE AND WATERBORNE DISEASES

I. Diseases typified by vomiting after a short incubation period with little or no fever

Agent	Incubation period	Clinical Syndrome	Pathophysiology	Characteristic Foods	Specimens
A. *Staphylococcus aureus*	30 min - 8 hours; usually 2-4 hours	Vomiting, diarrhea	preformed enterotoxin	sliced/chopped ham and meats, custards, cream fillings	Food: enterotoxin assay (FDA), culture for quantitation and phage typing of staph, gram stain Handlers: culture nares, skin, skin lesions, and phage type Staph. Cases: culture stool and vomitus, phage type Staph.
B. *Bacillus cereus*	1-6 hours	Vomiting; some patients with diarrhea; fever uncommon	? preformed enterotoxin	cooked rice	Food: culture for quantitation Cases: stool culture
C. Heavy metals • Antimony • Cadmium • Copper • Iron • Tin • Zinc	5min-8 hours; usually <1 hour	Vomiting, often metallic taste		foods and beverages prepared / stored / cooked in containers coated / lined / contaminated with offending metal	Toxicologic analysis of food container, vomitus, stomach contents, urine, blood, feces

http://www.cdc.gov/eis/casestudies/xoswego.401.303.compendium.pdf

II. Diseases typified by diarrhea after a moderate to long incubation period, often with fever

Agent	Incubation period	Clinical Syndrome	Pathophysiology	Characteristic Foods	Specimens
A. *Clostridium perfringens*	6-24 hours	Diarrhea, abdominal cramps; vomiting and fever uncommon	enterotoxin formed *in vivo*	meat, poultry	Food: enterotoxin assay done as research procedure by FDA, culture for quantitation and serotyping Cases: culture stool for quantitation and serotyping of *C. perfringens*; test for enterotoxin in stool. Controls: culture stool for quantitation and serotyping of *C. perfringens*
B. *Bacillus cereus*	6-24 hours	Diarrhea, abdominal cramps, and vomiting in some patients; fever uncommon	?enterotoxin	custards, cereals, puddings, sauces, meat loaf	Food: culture Cases: stool culture
C. *Vibrio parahemolyticus*	4-30 hours	Diarrhea	tissue invasion, ?enterotoxin	seafood	Food: culture on TCBS, serotype, Kanagawa test Cases: stool cultures on TCBS, serotype, Kanagawa test
D. Salmonella (non-tyhpoid)	6 hours-10 days; usually 6-48 hours	Diarrhea, often with fever and abdominal cramps	tissue invasion	poultry, eggs, meat, raw milk (cross-contamination important)	Food: culture with serotyping Cases: stool culture with serotyping Handlers: stool culture with serotyping as secondary consideration

II. Diseases typified by diarrhea after a moderate to long incubation period, often with fever - continued

Agent	Incubation period	Clinical Syndrome	Pathophysiology	Characteristic Foods	Specimens
E. Norovirus (formerly, "Norwalk-like viruses")	15-77 hours; usually 24-48 hours	Vomiting, cramps, diarrhea, headache, fever	unknown	raw or undercooked shellfish; water; many others	Detection of viral RNA in stool or vomitus by reverse transcriptase-polymerase chain reaction (RT-PCR)
F. Rotavirus	16-48 hours	Vomiting, chills, and diarrhea, especially in infants and children	unknown	foodborne transmission not well documents	Cases: stool examination by EM or ELISA; serology Food: culture and serotype
G. *Escherichia coli* enterotoxigenic (ETEC)	6-48 hours	Diarrhea, abdominal cramps, nausea; vomiting and fever less common	enterotoxin	uncooked vegetables, salads, water, cheese	Cases: stool culture; serotype and demonstration of enterotoxin production; invasiveness assay
H. *Escherichia coli* enteroinvasive (EIEC)	Variable	diarrhea (might be bloody), fever, abdominal cramps	tissue invasion	same as ETEC above	same as ETEC above
I. *Listeria monocytogenes* - Invasive Disease	2-6 weeks	Meningitis, neonatal sepsis, fever	?	Milk, soft cheeses	Food: culture, serotype Cases: stool / blood cultures, serotype, serology
Listeria monocytogenes, Diarrheal Disease	Unknown (3-70 days?)	Diarrhea, fever, abdominal cramps	?	Milk, soft cheeses	same as above
J. *Vibrio cholerae* non-01 and non-0139	1-5 days	Watery diarrhea	enterotoxin formed *in vivo*,, ?tissue invasion	shellfish	Food: culture on TCBS, serotype Cases: stool cultures on TCBS, serotype

Agent	Incubation period	Clinical Syndrome	Pathophysiology	Characteristic Foods	Specimens
K. *Vibrio cholerae* O1 or 0139	1-5 days	Watery diarrhea, often accompanied by vomiting	enterotoxin formed *in vivo*	shellfish, water or foods contaminated by infected person or obtained from contaminated environmental source	Food: culture on TCBS, serotype Cases: stool culture on TCBS, serotype
L. *Shigella* spp.	12 hours - 6 days; usually 2-4 days	Diarrhea (often bloody), often accompanied by fever and abdominal cramps	tissue invasion	foods contaminated by infected foodhandler; usually not foodborne	Food: culture and serotype Cases: stool culture and serotype Handlers: stool culture and serotype
M. *Escherichia coli* enterohemorrhagic (*E. coli* O157:H7 and others)	1-10 days; usually 3-4 days	Diarrhea (often bloody), abdominal cramps (often severe), little or no fever	cytotoxin	beef, raw milk, water, apple cider, lettuce	Cases: stool culture on sorbitol-MacConkey; isolation of *E. coli* 0157:H7 or other Shiga-like toxin-producing *E. coli* from clinical specimen
N. *Yersinia enterocolitica*	1-10 days; usually 4-6 days	Diarrhea, abdominal pain (often severe)	tissue invasion, ?enterotoxin	pork products, milk, food contaminated by infected human or animal	Food: culture on CIN agar, cold enrichment Cases: stool culture on CIN
O. *Cyclospora cayetanensis*	1-11 days; median: 7 days	Fatigue, protracted diarrhea, often relapsing	tissue invasion	raw produce; water	Food/water: consult DPD Cases: stool examination for organisms; PCR (developmental) and testing for oocyste sporulation at DPD
P. *Cryptosporidium parvum*	2-28 days; median: 7 days	Diarrhea, nausea, vomiting; fever	tissue invasion	uncooked foods; water	Food/water: consult DPD Cases: stool examination for organisms or antigen; PCR and serologic test developmental (consult DPD)
Q. *Giardia lamblia*	3-25 days; median: 7 days	Diarrhea, gas, cramps, nausea, fatigue	?	uncooked foods; water	Food/water: consult DPD Cases: detection of antigen or organism in stool, duodenal contents, or small-bowel biopsy specimen

IV. Diseases most readily diagnosed from history of eating a particular type of food

Agent	Incubation period	Clinical Syndrome	Pathophysiology	Characteristic Foods	Specimens
A. Poisonous mushrooms	variable	Usually vomiting and diarrhea, other symptoms differ with toxin		wild mushrooms	Food: speciation by mycetologist
B. Other poisonous plants	variable	variable		wild plant	Cases: vomitus, blood, urine. Food: speciation by botanist; stool may sometimes be helpful in confirmation.
C. Scombroid toxin (histamine)	1 min-3 hours; usually <1 hour	Flushing, dizziness, burning of mouth and throat, headache, gastrointestinal symptoms, urticaria, and generalized pruritus	histamine	scombroid fish (tuna, mackeral, etc.); mahi-mahi, others	Food: histamine levels
D. Ciguatoxin	1-48 hours; usually 2-8 hours	Usually GI symptoms (diarrhea, nausea, vomiting) followed by neurologic symptoms (including paresthesia of lips, tongue, throat, or extremities) and reversal of hot and	ciguatoxin	large ocean fish, e.g., grouper, barracuda	Food: stick test for ciguatoxin (not widely available)
E. Paralytic shellfish poisoning	< 1 hour	vomiting, diarrhea, paresthesias of face and extremities, sometimes more severe neurologic symptoms	saxitoxin	mussels, clams, scallops, oysters	Food: Detection of toxin in epidemiologically implicated food
F. Pufferfish poisoning (tetrodotoxin)	10 min - 3 hours	Nausea, vomiting, paresthesias, dizziness, may progress to paralysis and death in hours	tetrodotoxin	pufferfish, others	Food: Detection of toxin in epidemiologically implicated food

Prevention – Food and Water

- Boil it, cook it, peel it, or forget it
- Avoid ice
- Wash hand when possible
- Condiments on table can be contaminated
- It is difficult to do .... but have to

Rifaximin and Chemoprophylaxis of Travelers' Diarrhea

Pros

- Poorly adsorbed oral antibiotic
  - Absent side effects
- Low levels of rifaximin resistance among enteric pathogens
- Prophylaxis against travelers' diarrhea for short-term travelers
  - ETEC predominant regions
  - ≥70% protection conferred

Cons

- Limited studies to date
  - Geographically delimited
  - Predominance of ETEC/EAEC
  - Short duration travel
- Impact of widespread usage for prophylaxis unknown

Prevention of Enteric Diseases in Deployed Personnel

- Pre-deployment counseling of troops
  - Avoid exposure to pathogens transmitted by soiled food and drink
  - Seek early treatment with diarrhea

- Administer appropriate enteric vaccines
  - Typhoid vaccines (oral or IM)
  - Hepatitis A vaccine [Havrix, Avaxim]; Hepatitis B vaccine

- Probiotics
  - No official recommendation

- Antibiotic chemoprophylaxis
  - Not recommended for routine travel or deployment

Thank You